A Three-Dimensional Computational Model of Action Potential Propagation Through a Network of Individual Cells.

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State of the art and current issues

- Well-known models (bidomain, monodomain) are homogenized;
- Assumed periodicity;
- Some specific issues (disorganization in the tissue) at the microscopic scale are arrhythmia-prone (DeBakker 1993);
- Need for a “microscopic” computational model.

Geometry of the problem and equations

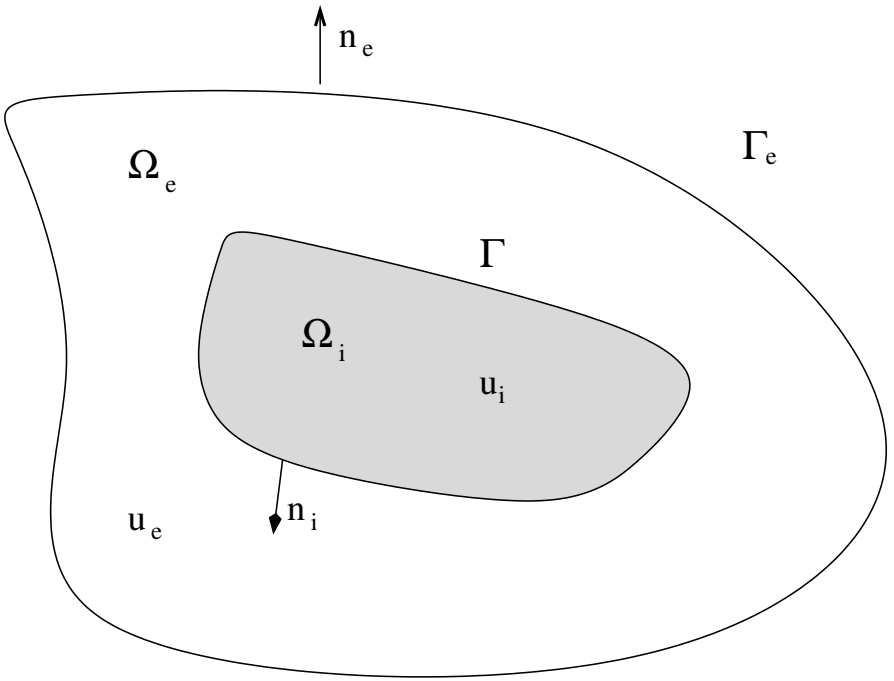


Figure: Basic geometry of the problem

$$
\begin{aligned}
-\sigma_i \Delta u_i &= 0 && \Omega_i \\
-\sigma_e \Delta u_e &= 0 && \Omega_e \\
-\sigma_i \nabla u_i \cdot n_i &= \sigma_e \nabla u_e \cdot n_e && \Gamma \\
c_m \partial_t(v) + I_{\text{ion}}(v) &= -\sigma_i \nabla u_i \cdot n_i && \Gamma \\
\sigma_e \nabla u_e \cdot n_e &= 0 && \Gamma_e
\end{aligned}
\tag{1}
$$

- Nonlinearities on the border of the cell (ionic model)
- Only v^0 provided as initial data
- Pure Neumann problem

This problem has a weak solution

Assembly 1/2 - Variational formulation

We use a P1-Lagrange finite element method with semi-implicit Euler time-stepping method

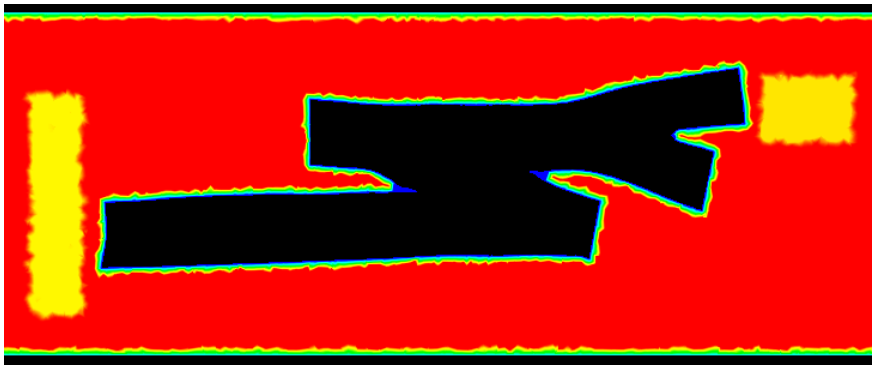
$$
\begin{cases}
\displaystyle\int_{\Omega_i} \sigma_i \nabla u_i^n \cdot \nabla \varphi_i \mathrm{d}x + \int_\Sigma \left[c_m \frac{u_i^n - u_e^n}{\delta t} + I_{\mathrm{ion}}(v^{n-1}) \right] \varphi_i \mathrm{d}s \\
\qquad\qquad = \displaystyle\int_\Sigma c_m \frac{v^{n-1}}{\delta t} \varphi_i \mathrm{d}s \\
\displaystyle\int_{\Omega_e} \sigma_e \nabla u_e^n \cdot \nabla \varphi_e \mathrm{d}x - \int_\Sigma \left[c_m \frac{u_i^n - u_e^n}{\delta t} + I_{\mathrm{ion}}(v_e^{n-1}) \right] \varphi_e \mathrm{d}s \\
\qquad\qquad = - \displaystyle\int_\Sigma c_m \frac{v^{n-1}}{\delta t} \varphi_e \mathrm{d}s
\end{cases}
$$

Assembly 2/2 - Linear system

$$\begin{pmatrix} A_{i,i}^n & A_{e,i}^n \\ A_{i,e}^n & A_{e,e}^n \end{pmatrix} \begin{pmatrix} U_i^n \\ U_e^n \end{pmatrix} = F_{\text{ion}}^{n-1} + F_{\text{time}}^{n-1}$$

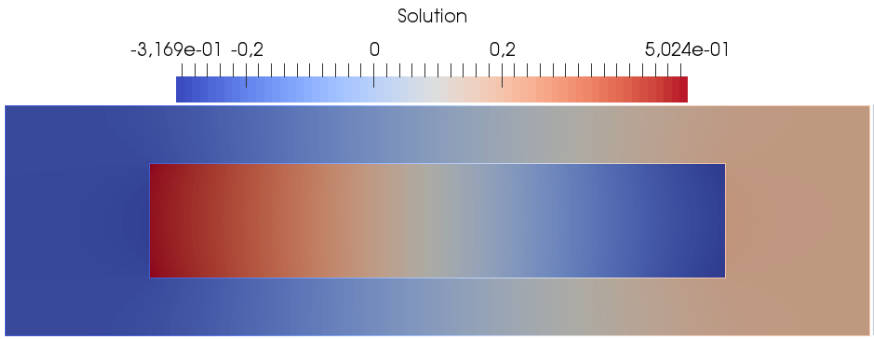
- Combination of stiffness part on the volume, mass part on the membrane and coupled terms (on $A_{i,e}$ and $A_{e,i}$);
- Ill-conditionned problem;
- We split the mesh in two parts (intra- and extracellular) and duplicate nodes on the membrane;

Simulation protocol

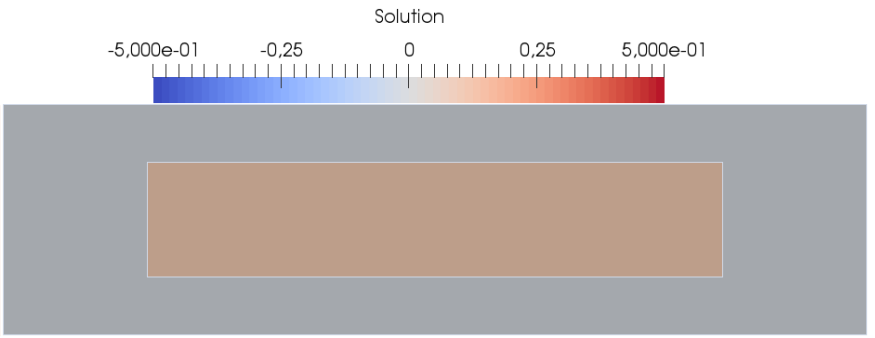


- Arbitrary stimulation at $t = 0.1ms$ for $0.02ms$ between an anode and a cathode;
- Use of Mitchell-Schaeffer model;
- 2D cases: cells are $100 \times 20\mu m^2$, 3D case: three cells embedded in a domain of size $300 \times 100 \times 70\mu m^3$;
- Extra/intracellular conductivity ratio is 1.75.

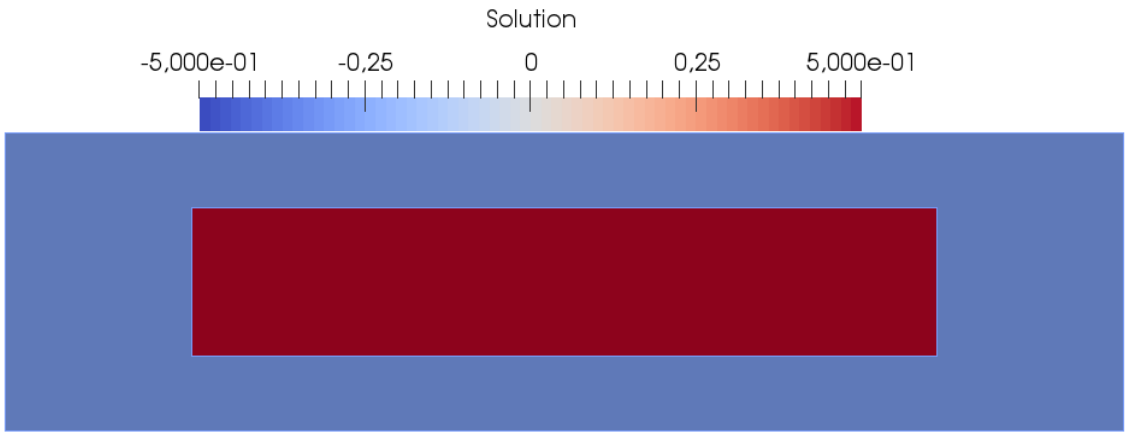
2D simulation - Single Cell



(a) Potential field at $t = 0.15$ms



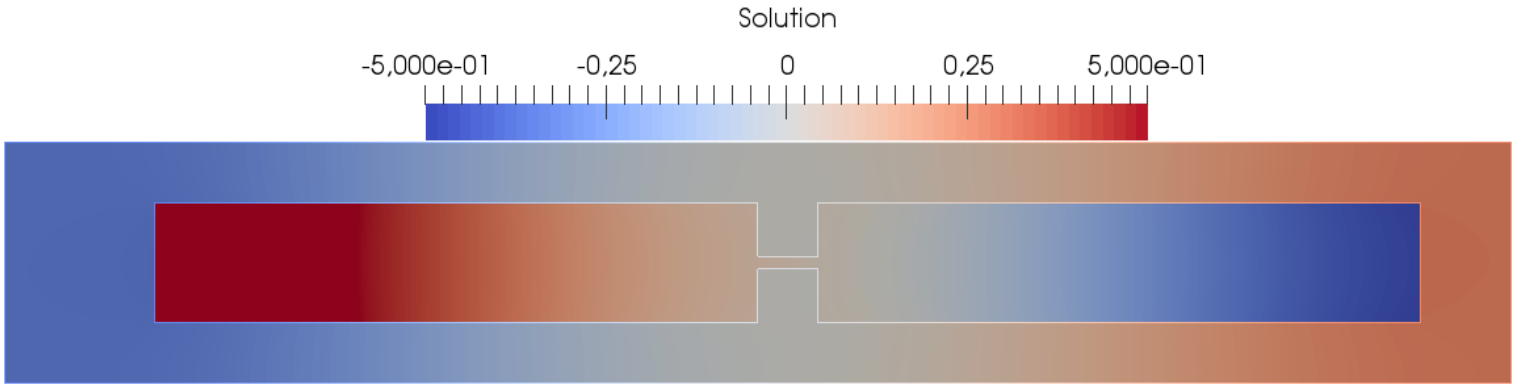
(b) Potential field at $t = 0.40$ms



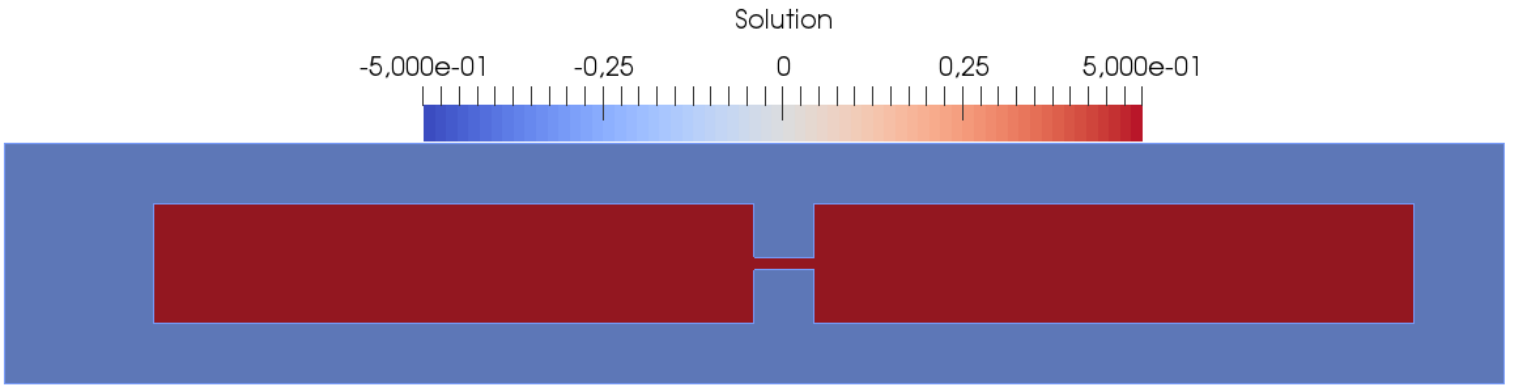
(c) Potential field at $t = 5.0$ms

Figure: First test case with a single cell, with an initial stimulation of intensity $I = 4.6$.

2D simulation - Two connected cells



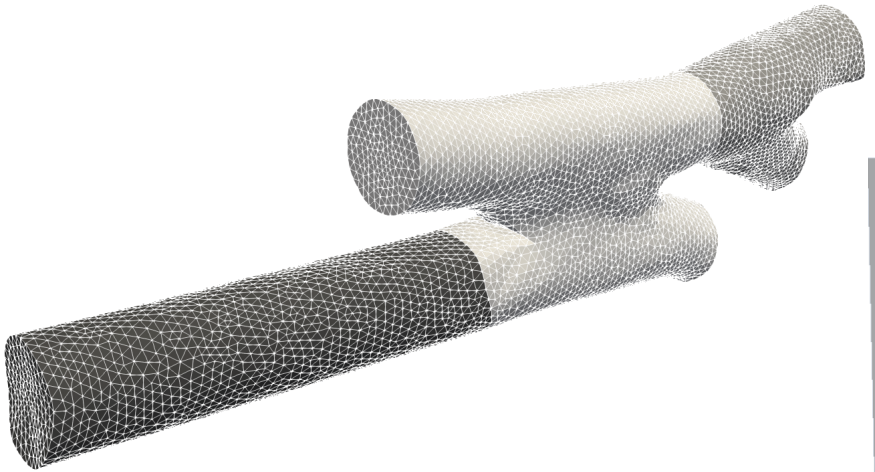
(a) Potential field at $t = 0.15$ms



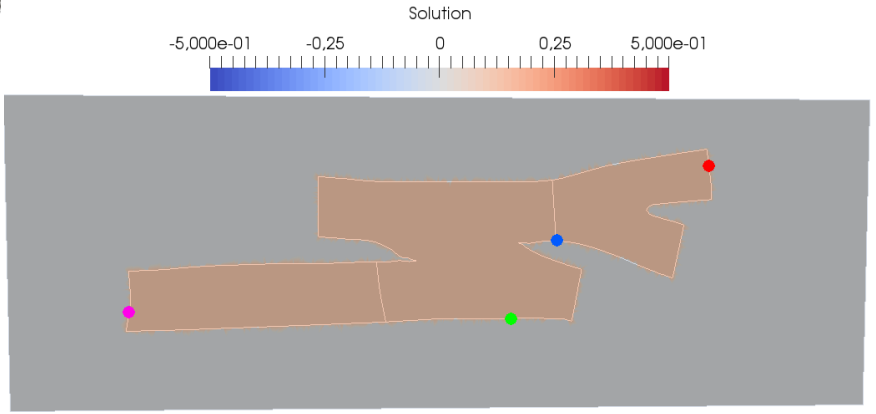
(b) Potential field at $t = 5.0$ms

Figure: Second test case with two connected cells, with an initial stimulation of intensity $I = 11.0$. The channel dimensions are $10 \times 2\mu m^2$.

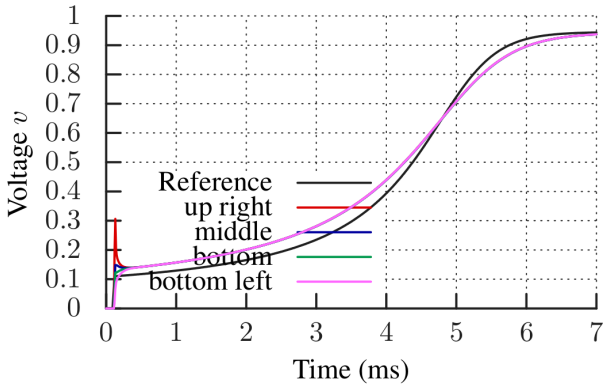
3D simulation



(a) Surface of the cells for the 3D case.



(b) Potential field at $t = 0.4$ms



(c) Depolarization process on the 4 colored points.

- 1.2M elements;
- 214k nodes;
- 40 000 steps;
- 4 3.3 GHz CPUs;
- 53.2h (whole AP).

Conclusion and further work

- A numerical solver of the microscopic bidomain model;
- It works in 2D and 3D;
- CPU time is reasonable.

- Build larger network of cells (in 2D) to test the propagation of the action potential;
- Implement a more accurate gap-junction model (Davidovic, CinC 2015);
- Test the scaling on clusters.